

**REMARKS**

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 112, are respectfully requested.

**Status**

Applicants' Request for Continued Examination ("RCE") has been granted and Applicants' submission dated July 22, 2003, has been entered. *See Official Action mailed September 29, 2003, Page 2.*

As is correctly reflected in the Office Action Summary, Claims 1, 6-11, 13, 14, 16-23, and 25-49 are pending. *Id.* Claims 1, 6-11, 13, 14, 16-23, and 25-49 stand rejected. *Id.* Acknowledgement was made in Paper No. 11 (mailed October 10, 2001) to Applicants' claim for foreign priority under 35 U.S.C. § 119(a)-(d) and all certified copies of the priority documents have been received in this national stage application from the International Bureau. *See Official Action mailed October 10, 2001, Office Action Summary.*

**Summary of Amendments**

By the foregoing amendments, Claims 1, 6-11, 13, 14, 16-23, 25, 26, 28, 41-44, and 46 were cancelled, without prejudice or disclaimer to Applicants filing one or more continuing applications directed to the previously-presented subject matter contained therein.

Also by the foregoing amendments, Claim 27 was amended to change its dependency to Claim 49 or Claim 51, as the claim from which it formerly depended was cancelled.

Also by the foregoing amendments, Claims 29, 48, and 49 have been amended to clarify that there are cleavage sites between the protective peptide, the helper peptide, and the peptide of interest so that the fusion protein formed by said peptides contains two cleavage sites. Support for this amendment may be found at least at Page 15, Line 12 to Page 17, Line 37 of the Specification and in Figure 7. Accordingly, no new matter has been added.

Also by the foregoing amendments, Claim 34 has been amended to correct a minor and typographical error. Specifically, step (5) has been corrected to read step (4), as Claim 29, from which Claim 34 depends, contains only four (4) steps. Accordingly, no new matter has been added.

Also by the foregoing amendments, Claims 38, 39, 40, and 45 have been amended to eliminate the abbreviation "GLP-1" and to add the full phrase "glucagon-like peptide-1." Support for this amendment may be found at least at Page 2, Lines 20-23 of the Specification ("... there can be mentioned human glucagon-like peptide-1 (referred to hereinafter as GLP-1 ..."). Accordingly, no new matter has been added.

Also by the foregoing amendments, Claims 29, 48, and 49 have been amended to clarify that the protective peptide is added to the peptide of interest-helper peptide unit. Support for this amendment may be found at least at Page 5,

Line 26 to Page 6, Line 15 of the Specification and in Figures 7 and 11-13.

Accordingly, no new matter has been added.

Finally by the foregoing amendments, Claims 51-53 have been added. Claim 51 depends from previously-presented Claim 49, and specifies that the peptide of interest is a glucagon-like peptide-1 derivative. Claim 52 depends from previously-presented Claim 29, and specifies that the fusion protein comprises a protective peptide-helper peptide-peptide of interest, in that order from N-terminal to C-terminal. Claim 53 depends from previously-presented Claim 47, and specifies that the modification reaction is an amidation. Support for these claims can be found at least at Page 20, Lines 27-37; Figure 1; and Page 17, Lines 21-28, respectively, of the Specification. Accordingly, no new matter has been added.

#### **Objections to the Specification**

The Examiner has objected to the Specification as purportedly failing to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. *See Official Action mailed September 29, 2003, Pages 2-3.* Applicants respectfully assert that these objections have issued in error.

The sequence "RHHGP[G]" is not an amino acid sequence, but instead a symbol of a peptide. This is explained at Page 21, Lines 5-13 of the Specification. Accordingly, no correction is warranted.

**Objections to Claims 14, 16, 17, 22, and 38-40 Due to Informalities**

Claims 14, 16, 17, 21, 22, and 38-40 were objected to for informalities such as the use of "GLP-1" and "and/orasalt." See *Official Action mailed September 29, 2003, Pages 4-5*.

Not to acquiesce in the Examiner's objections, but solely to facilitate prosecution, Applicants have cancelled Claims 14, 16, 17, 21, and 22 without prejudice or disclaimer. Such cancellation has rendered moot the corresponding foregoing objections.

With respect to Claims 38-40, these claims have been amended to delete the abbreviation "GLP-1" and to add the phrase "glucagon-like peptide-1." Accordingly, this objection has also been rendered moot by the foregoing amendments.

**Rejection Under 35 U.S.C. § 112, First Paragraph — Written Description**

Claims 1, 6-11, 13, 14, 16-23, and 25-49 have been rejected under 35 U.S.C. § 112, First Paragraph, as purportedly violating the written description requirement. See *Official Action mailed September 29, 2003, Pages 5-7*. This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, by the foregoing amendments Applicants have cancelled Claims 1, 6-11, 13, 14, 16-23, 25, 26, 28, 41-44, and 46. Accordingly, such cancellation has rendered moot the respective rejections.

Regarding remaining Claims 27, 29-40, 45, and 47-49, it must be kept in mind that "[w]hat is conventional or well known to one of ordinary skill in the art need not

be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) . . . " *M.P.E.P.* § 2163.

Applicants respectfully assert that a skilled artisan would have readily appreciated that Applicants were in possession of the subject matter claimed in Claims 27, 29-40, 45, and 47-49. The main characteristic of the instant invention is to transiently change a physicochemical property of a peptide of interest by adding a helper peptide to the peptide of interest, resulting in enhancement of yield and efficiency of recovery and purification of the peptide of interest. Therefore, a person with ordinary skill in the art can easily select a helper peptide dependent on a property to be changed to improve the yield and efficiency of recovery and purification of the peptide of interest. The properties to be provided to a peptide of interest are, for example, acidity, basic property, hydrophobicity, hydrophilicity, etc. For example, in the case of GLP-1, this peptide is acidic and is easily precipitated in an acidic condition, resulting in lower recovery of the peptide of interest. In this case, a basic helper peptide is selected.

The Examiner has also objected that the structure of GLP-1 is not disclosed in the Specification. See *Official Action mailed September 29, 2003, Page 7*.

Applicants respectfully assert that recitation of the structure of GLP-1 is not

necessary, as this peptide is well known. Moreover, the Specification explains that GLP-1 is described in the publication authored by Bell et al. in 304 NATURE 368-371 (1983). *See, e.g., Specification, Page 2, Lines 20-25.* Because, as indicated above, what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail, Applicants respectfully assert that the information provided in the Specification regarding GLP-1 is sufficient.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 112, First Paragraph, written description rejection of Claims 1, 6-11, 13, 14, 16-23, and 25-49.

**Rejection Under 35 U.S.C. § 112, First Paragraph – Enablement**

Claims 1, 6-11, 13, 14, 16-23, and 25-49 were rejected under 35 U.S.C. § 112, First Paragraph, as purportedly not enabled. *See Official Action mailed September 29, 2003, Pages 7-9.* This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, by the foregoing amendments Applicants have cancelled Claims 1, 6-11, 13, 14, 16-23, 25, 26, 28, 41-44, and 46. Accordingly, such cancellation has rendered moot the respective rejections.

Regarding remaining Claims 27, 29-40, 45, and 47-49, the inquiry is not whether experimentation is necessary, but whether, if experimentation is necessary, it is undue. *See M.P.E.P. § 2164.01.* Applicants respectfully assert that undue experimentation is not necessary to arrive at the subject matter claimed in Claims 27, 29-40, 45, and 47-49.

As admitted by the Examiner, the Specification enables a process for making GLP-1 using fusion proteins shown at Figures 11-13 and for making a highly-purified GLP-1. *See Official Action mailed September 29, 2003, Pages 7-9.* Applicants assert that those skilled in the art could readily call upon their skill and the information contained in the Specification to expand upon the recited principles to make and use the subject matter claimed in Claims 27, 29-40, 45, and 47-49.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 112, First Paragraph, enablement rejection of Claims 1, 6-11, 13, 14, 16-23, and 25-49.

**Rejection Under 35 U.S.C. § 112, Second Paragraph – Indefiniteness**

Claims 1, 6-11, 13, 14, 16-23, and 25-49 were rejected under 35 U.S.C. § 112, Second Paragraph, as purportedly indefinite. This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, by the foregoing amendments Applicants have cancelled Claims 1, 6-11, 13, 14, 16-23, 25, 26, 28, 41-44, and 46. Accordingly, such cancellation has rendered moot the respective rejections.

With respect to remaining Claims 27, 29-40, 45, and 47-49, not to acquiesce in the Examiner's rejection, but solely to facility prosecution, amendments were made which clarify the subject matter contained therein. Applicants respectfully assert that these amendments have rendered moot the foregoing indefiniteness rejections, and respectfully request withdrawal thereof.

**Rejection Under 35 U.S.C. § 102 (b) –Tarnowski**

Claims 1, 6-11, 13, 18-23, 25-27, and 41-44 were rejected under 35 U.S.C. § 102(b) as purportedly anticipated by U.S. Patent No. 5,202,239 to Tarnowski et al. ("Tarnowski"). *See Official Action mailed September 29, 2003, Pages 11-12.* This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, Applicants have cancelled Claims 1, 6-11, 13, 18-23, 25, 26, and 41-44. Applicants believe that these cancellations have rendered moot all of the rejections over Tarnowski but for the rejection of Claim 27. However, Claim 27, by the foregoing amendments, has been amended to depend from Claim 49, which does not stand rejected over Tarnowski. As a result, Applicants believe this rejection has also been rendered moot.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection of Claims 1, 6-11, 13, 18-23, 25-27, and 41-44 over Tarnowski.

**Rejection Under 35 U.S.C. § 103(a) – Tarnowski in View of Bell**

Claims 14, 16, 17, and 22 were rejected under 35 U.S.C. § 103(a) as allegedly over Tarnowski in view of Bell et al., 304 NATURE 368-371 (1983) ("Bell"). *See Official Action mailed September 29, 2003, Pages 12-13.* This rejection is respectfully traversed.



Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, Applicants have cancelled Claims 14, 16, 17, and 22, without prejudice or disclaimer. Applicants believe this has rendered moot the outstanding 35 U.S.C. § 103(a) rejection of Claims 14, 16, 17, and 22 over Tarnowski in view of Bell and withdrawal of said rejection is respectfully requested.

**Rejection Under 35 U.S.C. § 103(a) — Tarnowski in View of Mojsov et al.**

Claim 28 was rejected under 35 U.S.C. § 103(a) as purportedly obvious over Tarnowski in view of Mosjov et al., 79(2) JOURNAL OF CLINICAL INVESTIGATION 616-619 (1987) ("Mosjov"). This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, Applicants have cancelled Claim 28 without prejudice or disclaimer. Applicants believe this has rendered moot the outstanding 35 U.S.C. § 103(a) rejection of Claim 28 over Tarnowski in view of Mosjov, and withdrawal of said rejection is respectfully requested.

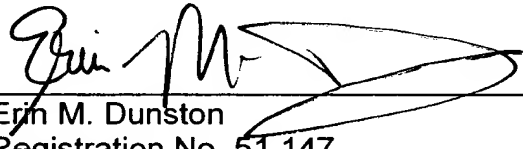
**CONCLUSION**

From the foregoing, further and favorable consideration in the form of a Notice of Allowance is respectfully requested and earnestly solicited.

In the event that there are any questions relating to this response, or the application in general, it would be greatly appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,  
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: \_\_\_\_\_

  
Erin M. Dunston  
Registration No. 51,147

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

Date: March 29, 2004